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EXAMINER	
ARCHIE, NINA	

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1645	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/585,721	DUBREMETZ ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/12/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office is responsive to Applicant's amendment and response filed 2-26-09. Claims 1-6 are pending and under examination.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority based on application filed on 7/12/2006. It is noted, however, that applicant has not filed a certified copy of the application as required by 35 U.S.C. 119(b).

Drawings

3. The drawings in this application have been accepted. No further action by Applicant is required.

Specification

4. The use of the trademarks for example, Quickchange ® (pg. 18 line 19), Lipofectamine ® (see page 19 line 5 for example), and TOXOVAX ® has been noted in this application. However, it should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

5. The information disclosure statement filed on 7/12/2006 has been considered. An initialed copy is enclosed.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 4-5 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a well established utility.

Claims 4-5 provides for the use of a mutant strain as claimed in any one of claims 1 to 3, for obtaining a vaccine (claim 4); The use as claimed in claim 4 characterized in that said vaccine is an anti-toxoplasmosis vaccine (claim 5); but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 4-5 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 112

> The following is a quotation of the first paragraph of 35 U.S.C. 112:
> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the reduction of febrile abortions caused by *T.*

gondii through the administration of the mic1-3KO mutant does not provide enablement for any vaccine comprising a mutant strain of an Apicomplex of the family *Sarcocystidae*, characterized in that it comprises a mutation which inactivates the adhesin MICI and a mutation which inactivates the adhesin MIC3 (claim 1), wherein the strain is Toxoplasma (claim 2), wherein the strain is Toxoplasma gondii (claim 3). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Enablement is considered in view of the Wands factors (MPEP 2164.01 (A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

(A) The nature of the invention;

(B) The breadth of the claims;

(C) The state of the prior art;

(D) The level of one of ordinary skill;

(E) The level of predictability in the art;

(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and

(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Nature of the invention: The instant claims are drawn to a vaccine comprising a mutant strain of an Apicomplex of the family *Sarcocystidae*, characterized in that it comprises a mutation which inactivates the adhesin MICI and a mutation which inactivates the adhesin MIC3 (claim 1), wherein the strain is *Toxoplasma* (claim 2), wherein the strain is *Toxoplasma gondii* (claim 3).

Breadth of the claims: The claims encompass all vaccines comprising a mutant strain from any species of an *Apicomplex* family of *Sarcocystidae* which encompass,

Toxoplasma gondii, Besnoitia bennetti, Besnoitia besnoiti, Besnoitia tarandi, Sarcocystis, and Neospora. The claimed invention is not limited to a particular vaccine. Since the specification fails to provide particular guidance for any particular vaccine, it would require undue experimentation to practice the invention over the scope as presently claimed.

Guidance of the specification/The existence of working examples: The specification discloses, mice immunized with a mutant, wherein MIC1 and MIC3 were inactivated (mic1-3KO mutant) (see pg. 12 and Example 4). The specification discloses the mice form virtually no brain cyst during a reinfection with the Toxoplasma gondii strain 76K with a 99.9% protection. The specification discloses ewes immunized with mic1-3KO (see pgs. 28-30). The specification discloses female ewes were infected with oocysts of PRU strain at mid-gestation and the results of febrile and infectious abortions were recorded (see pg. 30 lines 20-30). The specification displays the reduction of febrile abortions (see pg. 34 Table III Example 5, pg. 37). No data regarding the induction of a protective immune response to a given pathogen was disclosed. Thus the specification is only limited to the reduction of febrile abortions caused by *Toxoplasma gondii* through the administration of the mic1-3KO mutant.

The data as set forth supra does not demonstrate that the composition confers "protection" against infection by Toxoplasma gondii. The data merely shows that said composition reduces the number of mice and ewes dying from Toxoplasma gondii. Furthermore the specification discloses data only for Toxoplasma gondii strain. Therefore the data fails to show treatment or vaccine protection against any other species within the *Sarcocystidae* family. Therefore, one skilled in the art would not accept on its face the examples given in the specification as being correlative or representative of a successful model. The working examples do not disclose any empirical data or results indicative of a vaccine comprising a mutant strain as claimed.

The specification does not disclose any working example that any vaccine aforementioned above will work against infection nor vaccine protection with mic1-3KO. A vaccine by definition must provide protection against an infection demonstrable by challenge experiments. The specification is devoid of any teaching that the claimed

vaccine provides with any strain of Apicomplex family discloses a protective response against any subject.

The specification discloses, mice immunized with a mutant, wherein MIC1 and MIC3 were inactivated (mic1-3KO mutant) (see pg. 12 and Example 4) which indicate antibody response (see pg. 25). The specification discloses ewes immunized with mic1-3KO which indicate antibody response (see pgs. 28-31) and reduced the number of abortions (see pg. 34 Table III Example 5). The specification discloses vaccine protection mic1-3KO which shows zero protection (see pg. 37). The data as set forth supra does not demonstrate that the composition confers "protection" against infection by *Toxoplasma gondii* or any other pathogen. It merely shows that said composition reduces the number of mice and ewes dying from *Toxoplasma gondii*. Furthermore the specification discloses data only for *Toxoplasma gondi*n. The specification does not disclose any working example that any vaccine, comprising a mutant strain of an Apicomplex of the family Sarcocystidae, characterized in that it comprises a mutation which inactivates the adhesin MIC1 and a mutation which inactivates the adhesin MIC3 (claim 1), wherein the strain is Toxoplasma (claim 2), wherein the strain is Toxoplasma gondii (claim 3). A vaccine by definition must provide protection against an infection demonstrable by challenge experiments. The specification is devoid of any teaching that the claimed vaccine provides with any strain of Apicomplex family discloses a protective response against any subject.

State of the art: Although many investigators have tried to develop vaccines based on specific antigens, it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection (Chandrashekar et al., US Patent 6,248,329, col. 1, lines 35-41). It is well recognized in the vaccine art, that it is unclear whether an antigen derived from a pathogen will elicit protective immunity. Ellis (Chapter 29 of Vaccines, Plotkin, et al. (eds) WB Saunders, Philadelphia, 1998, especially p. 571, paragraph 2) exemplifies this problem in the recitation that "the key to the problem (of vaccine development) is the identification of

that protein component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.., and thus protect the host against attack by the pathogen." Moreover, protein chemistry is probably one of the most unpredictable areas of biotechnology. Consequently, the effects of sequence dissimilarities upon protein structure and function cannot be predicted. For the reasons set forth supra, the state of the art is has limitations to a vaccine composition and the state of the art is unpredictable with regard any vaccine comprising a mutant strain of an Apicomplex of the family *Sarcocystidae*, characterized in that it comprises a mutation which inactivates the adhesin MICI and a mutation which inactivates the adhesin MIC3 (claim 1), wherein the strain is *Toxoplasma* (claim 2), wherein the strain is *Toxoplasma gondii* (claim 3).

In conclusion, the claimed invention is enabled for the reduction of febrile abortions caused by *T. gondii* through the administration of the mic1-3KO mutant but does not provide enablement for any vaccine comprising a mutant strain of an Apicomplex of the family *Sarcocystidae*, characterized in that it comprises a mutation which inactivates the adhesin MICI and a mutation which inactivates the adhesin MIC3 (claim 1), wherein the strain is Toxoplasma (claim 2), wherein the strain is Toxoplasma gondii (claim 3). The claims encompass all vaccines of an Apicomplex family. The specification fails to teach that all mutant strains of an Aplicomplex family can produce a protective response in the host, as is requisite of a vaccine composition. The state of the art teaches that there are limitations to a vaccine composition and the state of the art is unpredictable. In view of the lack of support in the art and specification for an effective recombinant vaccine, it would require undue experimentation on the part of the skilled artisan to make and use the vaccine as claimed; therefore the claims are not enabled. As a result, for the reasons discussed above, it would require undue experimentation for one skilled in the art to use the claimed method.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claim 1-5 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As to independent claim 1 and dependent claims 2-3, the claims recite the indefinite article "characterize". The claims do not indicate that there is a limitation within the claim. Amendment of the claims to add the word "wherein" would make the claims clear and obviate this issue.

9. Claims 4-5 provides for the use of a mutant strain as claimed in any one of claims 1 to 3, for obtaining a vaccine (claim 4); The use as claimed in claim 4 characterized in that said vaccine is an anti-toxoplasmosis vaccine (claim 5); but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

10. Claims 1-3 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bassuny et al 2003 Infection and Immunity Vol. 71 No. 11 pgs.6222-6228, in view of Meissner et al 2002 Journal of Cell Science 115 pgs. 563-574.

The claims are drawn to a mutant strain of an Apicomplex of the family *Sarcocystidae*, characterized in that it comprises a mutation which inactivates the adhesin MIC1 and a mutation which inactivates the adhesin MIC3 (claim 1), wherein the strain is Toxoplasma (claim 2), wherein the strain is *Toxoplasma gondii* (claim 3).

Bassuny et al teach a mutant strain of *Toxoplasma gondii* comprising a plasmid encoding an immature form of the MIC3 protein (pMIC3i) (see abstract and pg. 6223 column 1) (claims 1-3).

Bassuny et al is relied upon as set forth supra however Bassuny et al does not teach a mutation which inactivates the adhesin MIC1 in a mutant strain .

Meissner et al teach a mutant strain mic1ko of Toxoplasma gondii (see 569 column 1 second paragraph and Figure 6) which correlates to a mutant strain comprising a mutation which inactivates the adhesin MIC1 (claims 1-3).

It would have been prima facie obvious at the time the invention was made to incorporate the mutant strain (mic1ko) MIC1 (as disclosed by Meissner et al) with the mutant strain (pMIC3i) MIC3 (as disclosed by Bassuny et al) in order to take advantage of the greatly decreased virulence *in vivo* associated with the double mutant strain.

One would have a reasonable expectation of success because a mutation which inactivates MIC3 (as disclosed Bassuny et al) (pMIC3i) combined with other relevant candidates for vaccination can enhance protection against the maladies associated with *Toxoplasma gondii* infection

Conclusion

10. Claims 1-3 and 6 are rejected and under examination.

Claims 4-5 are objected.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

/Robert A. Zeman/
for Nina Archie, Examiner of Art Unit 1645